

ABSTRACT

[0085] Novel lipid compounds are provided that may be termed "pro-cationic" in that they are neutral or negatively charged until they are either brought into contact with cellular membranes or are internalized by cells. The lipids have a hydrophobic tail group and a hydrophilic head group, the head group incorporating both a positively and negatively charged region at physiological pH. The hydrophobic tail group is stably connected to the positive region of the head group which in turn is connected to the negative region by a disulfide bond that is susceptible to cleavage by membrane-bound and intracellular factors. Cleavage of the disulfide bond removes the negatively charged region from the head group resulting in a lipid that is cationic and therefor fusogenic with negatively charged cell membranes. Consequently, lipids of the invention are useful as components of liposomes that serve as vehicles for delivering pharmaceutical agents into cells with reduced toxicity.

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